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08/448649

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/448,649	05/24/95	MASINOVSKY	B 27866/32663

EXAMINER	
GAMBEL, P	

18N1/0807

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ART UNIT	PAPER NUMBER
1816	21

DATE MAILED: 08/07/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 12/26/95, 5/24/95.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 30-33 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 30-33 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ tice of Draftsperson's Patent Drawing Review, PTO-948

☐ of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

★ U.S. GPO: 1996-410-238/40050

15. The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1816.

16. According to applicant's amendment, filed 12/26/95 (Paper No. 20), claim 30 has been amended.

Claims 1-29 have been canceled previously.
Claims 30-33 are pending and being acted upon presently.

17. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Action will be in response to applicant's arguments and amendments, filed 12/26/95 (Paper No. 20). The rejections of record can be found in the previous Office Action (Paper No. 17).

18. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the form PTO-948 previously sent in Paper No. 4.

19. Applicant should update the status and relationship of all parent applications on the first line of the specification.

20. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

21. The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure and failing to present the best mode contemplated by the applicant for carrying out the invention.

21. Claims 30-31 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: "a method of modulating interaction between a bone marrow stromal

cell and an immature bone marrow cell".

There does not appear to be support either for "a method of modulating interaction" nor "immature" bone marrow cell in the specification as-filed (see Example, 5 in particular). The specification discloses that applicant infers that adhesive interaction within the bone marrow between hemopoietic stem cell and/or progenitor cells and stromal elements may be mediated by VLA-4 and the antigen recognized by 6G10. The specification discloses that based upon binding and immunoprecipitation studies with 6G10 on culture human bone marrow stroma, one could use VCAM-1-specific binding partners or antibodies could be useful to modify in either a positive or negative fashion the growth or differentiation of bone marrow stem cells of bone marrow stroma. In contrast to applicant's current claimed recitation, there does not appear to be written support for "methods of modulating interaction" or "immature". The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed.

Applicant is required to cancel the new matter in the response to this Office action.

In view of additional rejections below, applicant is invited to recite the intended invention in a clear manner consistent with the specification as-filed.

22. Claims 30 and 32-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for VCAM-1-specific antibody 6G10 or antigen-binding specificities like 6G10 (Example 5) does not reasonably provide enablement for any other VCAM-1-specific antibodies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

The specification discloses that other VCAM-1-specific antibodies which recognize VCAM-1 on human endothelium do not bind significantly to human bone marrow stroma (Example 5). Therefore, the antigenic epitope recognized by the 6G10 antibody appears unique compared to other VCAM-1-specific antibodies.

As pointed in the last Office Action (Paper No. 17), Simmons et al. (Blood, 1992) teach that the instant VCAM-1-specific antibody 6G10 did not block the binding of hemopoietic progenitors in vitro (see entire document, particularly page 394, column 1).

Based upon in vitro inhibition assays, Liesveld et al. (Blood, 1993) discloses that antibodies to VCAM-1, VLA-4α or β1 or other VLA integrins completely inhibit myeloid progenitor adhesion to marrow stroma and in most cases, inhibition of adhesion noted was minimal (see entire document, particularly Discussion, page 118, column 2, paragraph 2).

Although integrins including VLA-VCAM can play a role in hemopoietic cell- bone marrow stroma interactions, such interactions are not necessarily predictive for the ability to modulate or decrease adhesion of said cells with any VCAM-1 specificity to achieve the therapeutic endpoint, commensurate in scope with the claimed invention.

The Papayanopoulou declaration under 37 C.F.R. § 1.132 filed 12/26/95 (Paper No. 20; Exhibit B) is sufficient to overcome the rejection of the instant claims 30-33 based upon 35 U.S.C. 112, first paragraph as it applies to the 6G10 specificity and the ability to decrease adhesion between bone marrow stromal cells and bone marrow cells to release hemopoietic progenitor cells.

The Torok-Storb declaration under 37 C.F.R. § 1.132 filed 12/26/95 (Paper No. 20; Exhibit C) is sufficient to overcome the rejection of the instant claims 30-33 based upon 35 U.S.C. 112, first paragraph as it applies to the use of decreasing adhesion between bone marrow stromal cells and bone marrow cells to release hemopoietic progenitor cells.

Applicant's arguments, filed 12/26/95 (Paper No. 20) have been fully considered but are not found convincing with respect to the breadth of the instant claims drawn to any VCAM-1-specific antibody. Applicant argues that VCAM-1 is specifically involved in adhesive interactions between stromal cells and hemopoietic cells. However, applicant's instant disclosure (Example 5) and the Papayanopoulou declaration clearly support distinctions between the 6G10 antibody specificity and other VCAM-1 specificities. Applicant's arguments are not consistent and commensurate in scope with applicant's own admission in the specification as-filed nor with the supporting evidence provided in the Papayanopoulou declaration. Applicant's arguments are not persuasive for the operability of any VCAM-1 specificity. Applicant is enabled only for the 6G10 antibody specificity.

23. Claims 30-33 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 30-33 are indefinite in the recitation of "modulating the interaction between a bone marrow stromal cell and an immature bone marrow cell" because the characteristics of "modulating" are not clear and ambiguous. Modulation can occur either as stimulation or inhibition, for example. Although the claimed method also recites "in an amount effective to decrease adhesion between the bone marrow stromal cell and the bone marrow cell"; this recitation does not indicate antecedent basis to "method of modulating interaction". Therefore, the "method of modulating interaction" can include other interactions and is not necessarily limited to a decrease in adhesion. There is insufficient direction or guidance is provided to one skilled in the art in the determination of any or all "methods of modulating interaction" between bone marrow cell and stromal cells in both a positive and negative fashion, as disclosed in Example 5 of the instant specification. Further, there is insufficient evidence or nexus provided that any VCAM-specific agents can modulate such interactions therapeutically, commensurate in scope with the claimed invention. It appears that undue experimentation would be required of one skilled in the art to practice the method of claim methods using the teaching of the specification alone.

Applicant should draft the method claims as inhibition or other appropriate terms that relate to the type of modulation enabled and indicate written support in the specification as-filed.

B) Claims 30-33 are indefinite in the recitation of "bone marrow stromal cell" and "immature bone marrow cell" because their characteristics are not known and the use of both phrases are ambiguous. Bone marrow stromal cells include a number of cell types including fibroblasts, endothelial cells, adipocytes and numerous hemopoietic cell elements. For example, macrophage or dendritic cells are often associated with the bone marrow stroma. It appears that applicant's recitation of "bone marrow cell", "stem cell" and "progenitor cell" is meant to refer to hemopoietic cells; but "hemopoietic" is not recited in the instant claims. Therefore, "bone marrow stromal cell" and "immature bone marrow cell" are ambiguous as they can overlap in comprising similar cell populations. Applicant should distinguish between stromal cells and hemopoietic cells and indicate written support in the specification as-filed. Although applicant discloses the 6G10 antibody binds stromal cells, it does not disclose which of the many types of stromal cells in bone marrow is detected with this antibody. Not all bone marrow stromal cells express the 6G10-specific epitope (or antigen). There is insufficient direction or guidance in the specification as-filed as to which bone marrow stromal cell is bound by the 6G10 antibody.

C) The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

24. Based upon applicant's amended claims and arguments, filed 12/26/95 (Paper No. 20), applicant's instant claims drawn to methods of inhibiting bone marrow stromal cell- bone marrow hemopoietic cell adhesive interactions is free of the prior art.

25. Claims 30-33 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21-24 of copending application USSN 08/486,480. Although the conflicting claims are not identical, they are not patentably distinct from each other because both are drawn to the same endpoint, that is, decreasing adhesion between the bone marrow stromal cell and the bone marrow cell. It appears that mobilizing bone marrow cells and modulating interactions between bone marrow are drawn to the same, nearly the same or very similar methods. Therefore, the claimed methods of decreasing adhesion between bone marrow cells and bone marrow stroma are not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. *In re Vogel*, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. § 1.78(d).

26. No claim allowed.

27. Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CMI Fax Center telephone number is (703) 308-4242 or (703) 305-7939.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.

Phillip Gambel, Ph.D.
Patent Examiner
August 5, 1996

DONALD E. ADAMS
PRIMARY EXAMINER
GROUP 1800